Remarks and Arguments

Claims 1, 4-8 and 11-19 were presented for examination. Claims 1 and 11 have been amended.

Claims 1, 4-8, and 11-19 have been rejected under 35 U.S.C. §112, first paragraph, for failing to comply with the written description requirement. In particular, claim 1 was amended to recite, in step (f), "measuring one of a substantially constant current and a substantially constant voltage". The examiner considers the "substantially constant" limitation to be unsupported by the specification as originally filed which does not specify what portion of galvanic cell current or voltage production is "substantially constant" and does not indicate that a particular portion of any current or voltage produced should be measured.

In response, claim 1 has been amended to remove the "substantially constant" limitation and to recite, in step (f), "…measuring one of a galvanic cell current and a galvanic cell voltage generated between the electrodes of the galvanic cell…" It is well-known that a galvanic cell generates known voltages and currents in a manner that is particular to such cells. Accordingly, it is believed that the current wording of claim 1 meets the requirements of 35 U.S.C. §112, first paragraph. Claims 4-8 and 11-19 have been rejected for their dependency on a rejected claim. Accordingly, the rejection of claims 1, 4-8 and 11-19 under 35 U.S.C. §112, first paragraph, is hereby respectfully traversed.

Claims 1, 4, 7, 8 and 11 have been rejected under 35 U.S.C. §103(a) as obvious over Wang (previously cited) in view of an article entitled "Galvanic Stripping - A Simple and Versatile Approach to Trace Analysis"' S. Jaya *et al.*, *Analytical Letters*, v. 18, n. 12, pp. 1441-1456, 1985 (Jaya) and Knoll (previously cited). The examiner comments that Wang discloses all of the claimed limitations with the exception that it does not specifically teach measuring a substantially constant current or voltage generated between the electrodes of a galvanic cell, as required by step (f) of claim 1. However, the examiner considers that such measurements were well known at the time the invention was made as evidenced by Jaya. Further the examiner indicates that the combination of Wang and Jaya does not teach immobilized probes, a method in which nanoparticles are bound to analytes before the analytes are hybridized to the capture probe or methods where the electrical contact between the nanoparticle and the contact spot is established by

electrically conductive molecules. However, the examiner considers that such methods for electrically-based nucleic acid detection were well known in the art at the time the invention was made as evidenced by Knoll.

The Wang and Knoll references have been discussed in detail in a previous response filed January 17, 2008. The Jaya reference discloses an anodic stripping process that is related to the potentiometric stripping process disclosed in Wang. In the Jaya process, instead of using a potential or a chemical process to strip a predeposited analyte from a working mercury electrode as disclosed in Wang, the electric circuit between the working electrode and a counterelectrode is left open in order to allow the analyte to spontaneously dissociate itself from the working electrode. The Jaya reference does disclose measuring the potential of the electrochemical cell during this process.

From the discussion above and the description of the Wang process in the response filed January 17, 2008, it is clear that, in the Wang and Jaya processes, the metal involved in the electrochemical cell is dissolved chemically (oxidation) and then the dissolved metal is deposited on the working electrode by applying electrical potentials to the electrodes of the setup (reduction). The oxidation and reduction processes are disclosed in Jaya, p. 1445, lines 14-24 which state:

> "The solution [of dissolved cadmium] was then electrolysed to accumulate cadmium metal on the MF GCE [mercury film glassy carbon electrode = working electrode] at -1.0 V vs. NCE [normal calomel electrode] for 4 minutes. Following this, the potential output was recorded on an X-Y recorder after keeping the potentiostat in E_R position (open Circuit Selection mode) to draw the E-t profiles that represent the time variations of the working electrode potential versus the reference electrode potential."

A similar process is described in Wang, p. 5578, left column, which states:

"**Chronopotentiometric Stripping Analysis**. Each experiment was carried out with a new electrode strip and included an initial background evaluation followed by the actual detection of the dissolved gold tag. PSA measurements were performed by cleaning the surface at +1.2 V for 3 min followed by a 2-min deposition at -0.8 V using a stirred 1.0 M HBr/0.l mM Br_2 solution. Subsequent stripping was performed in a quiescent solution after a

> 5-s rest period using an applied anodic current of +5.0 μA. The stripping curve data were filtered and baseline corrected with the TAP2 software."

This is in contrast to the present invention in which the electrical contact between the metal surfaces of the nanoparticles and the contact spot is established to form a galvanic cell without destroying the nanoparticles. Instead, the intact nanoparticles are used to form the contact. This difference is now specifically recited in claim 1, which has been amended in lines 13-16, to recite "…establishing an electrical contact between the metal surfaces on the nanoparticles and the contact spot without destroying the nanoparticles so that the counterelectrode and the metal surfaces of the intact nanoparticles form electrodes of a galvanic cell…" It is clear that neither Wang nor Jaya disclose such an arrangement. The Knoll reference has been discussed in detail in a previous response filed on February 6, 2007. There it was pointed out that, in the Knoll reference, the nanoparticles are electrically isolated and do not form one of the electrodes of a galvanic element. Thus, its combination with Wang and Jaya does not add the disclosure that is missing in Wang and Jaya. Consequently, amended claim 1 patentably distinguishes over the combination of Wang, Jaya and Knoll.

Claims 4, 7, 8 and 11 depend, either directly or indirectly on amended claim 1, and incorporate the limitations thereof. Therefore, these latter claims also patentably distinguish over the cited reference combination in the same manner as amended claim 1. In addition, these claims also recite limitations not disclosed or suggested by the cited combination of references. For example, claim 11 has been amended to recite that electrical contact between the nanoparticles and the contact spot is established by electrically conductive molecules other than the nanoparticles. The examiner points to Knoll, which indicates that the disclosed marker particles are conductive. However, in Knoll the marker particles correspond to the nanoparticles of the present invention. Thus, in Knoll, there are no other electrically conductive molecules as recited in claim 11.

Claims 6, 18 and 19 have again been rejected under 35 U.S.C. §103(a) as obvious over Wang, Jaya and Knoll in view of U.S. Patent No. 6,391,558 (Henkens, previously cited.) The examiner comments that the Wang, Jaya and Knoll references

disclose all of the claimed limitations with the exception that they do not explicitly disclose covalent binding for immobilizing the probe molecules as recited in claim 6 or PCR amplification as recited in claims 18 and 19. However, the examiner claims that the Henkens reference discloses both covalent binding and PCR techniques in conjunction with detection of nucleic acids using electrodes with immobilized probes.

As previously discussed, Henkens does not disclose the formation of a galvanic cell by intact nanoparticles as now recited in claim 1 on which claims 6, 18 and 19 depend. Thus, none of the Wang, Jaya and Knoll references nor the Henkens reference discloses the construction of such a galvanic cell.

Claims 5 and 12 have been rejected under 35 U.S.C. §103(a) as obvious over Wang, Jaya and Knoll in view of Wohlstadter (previously cited.) The examiner comments that Wang, Jaya and Knoll disclose the recited limitations with the exception that they do not disclose the use of polyene molecules to conduct electrical signals as recited in claims 5 and 12. However, the examiner indicates that Wohlstadter discloses such a use of a linking chain in the polyene class to insure low resistance transfer of electrons from an electrode.

As discussed above, the Wang, Jaya and Knoll references do not teach the formation of a galvanic cell as claimed in claim 1, the parent claim of claims 5 and 12. Adding Wohlstadter to this combination does not change this conclusion because Wohlstadter detects the presence and quantity of the analyte molecules by electrochemiluminescence, not by forming a galvanic cell and then measuring the electrical properties of that element as recited.

Claims 13, 16 and 17 have been rejected under 35 U.S.C. §103(a) as obvious over Wang, Jaya and Knoll in view of Fish (previously cited.) The examiner comments that Wang, Jaya and Knoll disclose the recited limitations with the exception that they do not disclose moving a countersurface to press nanoparticles against a contact spot, but the examiner indicates that Fish discloses the detection of analyte molecules with an electrode-based scheme in which an opposing surface with an electrode is moved to make contact with an electrically-readable particle.

The Fish reference has been discussed in detail in the previous response mentioned above. Combining Fish with Wang, Jaya and Knoll would not produce an

arrangement which forms a galvanic cell by means of intact nanoparticles because Wang, Jaya and Knoll do not disclose the recited galvanic cell and Fish detects the presence and quantity of the analyte molecules by measuring electrical changes in a measuring cell, not by forming a galvanic cell and then measuring the electrical properties of that element as recited. Since claims 13, 16 and 17 are dependent on amended claim 1 and incorporate the limitations thereof, they distinguish over the cited reference combination in the same manner as claim 1.

Claims 14 and 15 have been rejected under 35 U.S.C. §103(a) as obvious over Wang, Jaya and Knoll in view of Fish and further in view of Wohlstadter. The examiner comments that Wang, Jaya, Knoll and Fish disclose the recited limitations with the exception that they do not disclose that the analyte is collected on a surface opposite to the surface on which the detecting electrode is mounted. The examiner indicates that Wohlstadter discloses several electrode-based detection configurations in which an analyte is collected on a surface opposite to the surface on which the detecting electrode is mounted.

The combination of Wang, Jaya, Knoll and Fish has been discussed above and does not teach the formation of a galvanic cell as claimed. Adding Wohlstadter to this combination does not change this conclusion because Wohlstadter detects the presence and quantity of the analyte molecules by electrochemiluminescence, not by forming a galvanic cell and then measuring the electrical properties of that element as recited. Since claim 14 is dependent on amended claim 1 and incorporates the limitations thereof, it distinguishes over the cited reference combination in the same manner as claim 1.

In light of the forgoing amendments and remarks, this application is now believed in condition for allowance and a notice of allowance is earnestly solicited. If the examiner has any further questions regarding this amendment, he is invited to call

applicants' attorney at the number listed below. The examiner is hereby authorized to charge any fees or direct any payment under 37 C.F.R. §§1.17, 1.16 to Deposit Account number 50-3969.

Respectfully submitted

/paul e. kudirka/ Date: 2008-08-27

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